REMARKS

Favorable reconsideration of the subject application is respectfully requested in light of the above amendments and the following remarks. Claims 1-11 were pending. Claims 1-5 have been canceled. Claims 6 and 7 have been amended to incorporate the relevant subject matter from former Claim 1 (now canceled). Support for the amendments may be found throughout the instant specification. Therefore, claims 6-ll are now pending. The amendments are not to be construed as acquiescence with regard to the Action's rejections and are made without prejudice to prosecution of any subject matter removed or modified by amendment in a related divisional, continuation, or continuation-in-part application. No new matter has been added to the application.

Objection to Specification

Applicants thank the Examiner for noting the informalities of the specification that formed the basis of objection. Applicants have amended the specification as requested in the Office Action to correct the inadvertent typographical errors. Thus, Applicants respectfully submit the objection to the specification has been overcome, and request this objection be withdrawn.

Rejection under 35 U.S.C. §112, First Paragraph

Claims 1-11 stand rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement. In particular, the Action states the language "derived from" permits a peptide analogue of any size to be encompassed by the

claims. The Action further states the specification lacks structural features of the peptide analogues necessary to bind to MHC or treat multiple sclerosis, such that Applicants do not adequately disclose a representative number of species to possess the genus claimed.

Applicants respectfully traverse this ground for rejection and submit Claims 1-5 have been canceled. With regard to Claims 6-11, Applicants submit the specification discloses sufficient description of a representative number of species by actual reduction to practice, as well as by disclosing relevant, identifying characteristics such that one of skill in the art would readily appreciate the Applicants were in possession of the invention at the time the application was filed.

Applicants respectfully submit actual reduction to practice is not necessary in order to satisfy the written description requirement under 35 U.S.C. §112, first paragraph. Nonetheless, Applicants submit, in addition to the rest of the specification, eleven Examples are included that provide adequate support for the claimed invention. Specifically, Examples 4-7 (pages 17-21 of the instant specification) and the corresponding discussion at pages 8-11, present evidence of the ability of MBP peptide analogues to bind MHC on whole spleen cells, antigen presenting cells, lymph node cells and T cells. Applicants note these data include both *in vitro* and *in vivo* assessments. Furthermore, as described in Example 6 and Figure 3, ten different peptide analogues were synthesized and tested at varying doses in a T cell proliferation assay. Thus, the ability of multiple peptide analogues to bind multiple cell types, as measured by multiple doses, is evidence that one of skill in the art would easily appreciate Applicants, at the time the application was filed, possessed a representative number of species of the genus claimed.

Applicants submit support for treatment of multiple sclerosis can be found throughout the instant specification, but in particular at Examples 8-10 on pages 21-22. Applicants submit the written description requirement of 35 U.S.C. §112, first paragraph does not require human data for treatment of disease. Applicants submit the instant specification adequately discloses data in experimental animal models, and one of skill in the art would recognize the animal model EAE is regarded as an appropriate animal model for the human disease of multiple sclerosis.

In particular, Example 8 describes reversal of EAE in the rat model using the described MPB peptide analogue, and Example 9 discloses the MBP peptide analogues themselves do *not* induce EAE in the animal model. As indicated in Example 10, the MBP peptide analogues of the claimed invention have the ability to prevent induction of EAE, whereas other peptide analogues, not presently claimed, *fail to prevent EAE induction.* Taken together, these cited examples support the presently claimed invention of a pharmaceutical composition and methods of treating multiple sclerosis.

Further, Applicants note on-going clinical trials, which began well before the filing date of the present application, are currently being conducted which utilize the presently claimed invention (*See* http://www.neurocrine.com/html/clin_multipleSclerosis.html). Briefly, a Phase II clinical study of multiple sclerosis patients is presently underway in order to evaluate the safety, tolerability and efficacy of an MBP peptide analogue encompassed by the presently claimed invention. Applicants' past clinical trials, conducted well before the filing date of the present application, were successful in using the MBP peptide analogue to treat patients with multiple sclerosis. Such success was measured by a reduction in new lesions as well as a reduction in total disease load, without exacerbation of disease. Applicants submit such on-

going clinical trials are further evidence that Applicants were in possession of the presently claimed invention, as required under 35 U.S.C.§ 112, first paragraph, at the time the application was filed .

In light of the evidence presented here, as well as the other evidence previously made of record (including the instant specification), Applicants submit one of skill in the art would easily appreciate Applicants were in possession of the claimed invention at the time the application was filed. Therefore, Applicants respectfully submit this ground for rejection has been overcome and request this rejection be withdrawn.

Rejection under 35 U.S.C. §102(b)

Claims 1-6 stand rejected under 35 U.S.C. §102(b) as alleged being anticipated by Martin *et al.* (J.Immunol. V. 148, pp. 1359-1366). In particular, the Action alleges Martin *et al.* teach peptides comprising residues 88-100 with the lysine at residue 91 altered to be alanine. The Action alleges the peptides of Martin *et al.* inherently reduce the expression of TNF-α from MBP-reactive T cells relative to the native sequence of MBP to the same extent claimed by Applicants because the Martin *et al.* peptides were used in cell *in vitro* cultures. The Action further alleges the cited reference anticipates Claims 1-6 because the peptides used in the *in vitro* cultures inherently must have been combined with a physiologically acceptable carrier or diluent.

Applicants respectfully traverse this ground for rejection, and submit Claims 1-5 have been canceled. Applicants note Claim 6 has been amended for clarification and now includes the subject matter of former Claim 1 (presently canceled). Applicants submit this amendment is made solely to expedite prosecution of the application and without acquiescing to any rejection.

As such, Applicants traverse this rejection of Claim 6 and assert Martin *et al.* does not anticipate the presently claimed invention since each and every element of the claims is not explicitly or inherently present in the cited reference. Applicants submit Martin *et al.* only examined peptides with a single alanine substitution in *in vitro* T cell cultures for antigen specificity assays. Applicants submit nothing in Martin *et al.* explicitly or inherently indicates a pharmaceutical composition of a peptide analogue as described in the presently claimed invention.

Regarding the Action's assertion that the peptides described in Martin *et al.* inherently must have been combined with a physiologically acceptable carrier or diluent, Applicants respectfully disagree. In particular, page 1360 of Martin *et al.* describes the manner in which the peptides were generated for all data indicated. Thus, the peptides utilized were only HPLC purified to a purity of approximately 95%, and were only utilized for *in vitro* purposes. As such, the final peptide preparations still contained contaminants (such as acetonitrile and blocked amino acids) and therefore, were clearly not suitable for pharmaceutical compositions or for administration to an animal, particularly for therapeutic purposes. Accordingly, Martin *et al.* do not disclose any peptide analogues other than alanine at position 91 and clearly do not disclose a pharmaceutical composition comprising a peptide analogue in combination with a physiologically acceptable carrier or diluent, according to the presently claimed invention.

Furthermore, Applicants submit the fact that a certain result or characteristic *may* occur or be present in a cited reference is not sufficient to establish the inherency of such result or characteristic when such is based on experimental data that includes optimization of conditions. *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPQ 1981). Applicants submit Example 8 and Example 10 disclose experimental evidence from animal models of

administration of peptide analogues in order to reverse and prevent EAE, respectively. Applicants submit one of skill in the art would not be able to take the peptides of Martin *et al.* and achieve the same results as Applicants' claimed invention without significant further experimentation and optimization. As such, Applicants submit Martin, *et al.* does not anticipate the presently claimed invention because each and every element of Claim 6 is not found *explicitly or inherently* in the cited reference. Therefore, Applicants respectfully submit this basis for rejection has been overcome and request the rejection be withdrawn.

Obviousness Type Double Patenting Rejection

Claims 1-6 stand rejected under the judicially created doctrine of obviousness-type double patenting as not patentable over U.S. Patent No. 6,740,638. Claims 1-11 stand rejected under the judicially created doctrine of obviousness type double patenting as not patentable over U.S. Patent No. 6,489,299 and U.S. Patent No. 6,369,033. Claims 1-5 stand rejected under the judicially created doctrine of obviousness-type double patenting as not patentable over U.S. Patent No. 6,329,499.

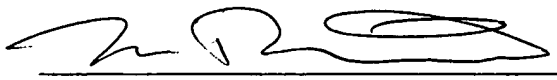
Applicants respectfully submit Claims 1-5 have been canceled. With regard to Claims 6-11, Applicants note the two terminal disclaimers filed April 8, 2004 in relation to U.S. Patent Nos. 6,740,638; 6,489,299; and 6,369,033 were not approved because they inadvertently lacked the "Application No." Applicants thank the Examiner for noting this unintentional error and note corrected terminal disclaimers are enclosed with this Response. Accordingly, Applicants respectfully request this rejection be reconsidered and withdrawn.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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